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[Extracted from the American Journal of the Medical Sciences for October, 1879.]

OBSERVATIONS ON INFILTRATION OF THE RETINA IN LARDACEOUS DISEASE OF THE KIDNEYS DUE TO CHRONIC SUPPURATION FROM BONE DISEASE.

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The connection between a certain variety of retinitis and chronic renal disease, and that between the latter and chronic suppuration from bone disease are two facts in pathology long since recognized. The latter fact has lately gained in importance owing to the recent discussion in England before the Pathological Society of London, upon the nature and causes of lardaceous disease or amyloid degeneration. In this discussion, though nothing very new was elicited, yet the recognition of two predominant causes, both alone and together, of lardaceous infiltration, viz.: chronic suppuration from bone caries and syphilis, was so unanimous as to aid materially in the further study of this branch of pathology.

Lardaceous disease of the eye and its appendages is of very rare occurrence, and has hitherto been described solely in the lids and conjunctiva. (See Virchow and Hirsch's *Jahresbericht*, 1873, Bd. I. p. 213. *Annali di Ottamologia*, VI. fasc. 2, p. 163. *Finska läkaresällskap*. Handl., 1875, p. 150 and 1876. *Archives of Ophthalmology*, VIII. No. 1. *Archiv für Ophthalmologie* Bd. XXV. Abth. 1.)

Certain peculiarities in two cases recently under the observation of the writer have excited a suspicion that lardaceous infiltration may possibly occur in the retina as the result of long-continued suppuration from bone-disease with chronic renal disease, primarily of a lardaceous nature. The suspicion has not become a certainty, for though death ensued in both cases, no autopsy could be obtained in either. The patients in both cases were young, and the histories are here given in detail.

Case I.—Margaret T., æt. 24, single, first seen in January 1879. No strumous taint discernible in any member of the family. No syphilis or rheumatism in the patient, but at the age of eighteen she suffered for nearly a year from malarial poisoning, which however finally disappeared and has never recurred. Eleven years ago, at the age of 13, the left leg was injured by a severe blow upon the crest of the tibia from a fall. This resulted in severe periostitis and necrosis of the bone, which has lasted ever since.

Two operations at different periods for the removal of the diseased bone were performed, with an interval of about a year, but both failed in putting a stop to the destructive process. For the past two years a spine or spicula of bone has protruded through the skin for nearly half an inch, at the junction of the upper and middle thirds of the tibia. This spicula is broad, thick, and roughened, the skin around the opening is livid and presents the ordinary signs of the presence of necrosed bone, and there is a constant thin purulent discharge from the opening. A probe passed in by the side of the protruding spine discovers dead bone in every direction.

During the past year the patient has been in constant ill-health. The menses have been very irregular in time and quantity, and during the past three months have been entirely suppressed. There have been an almost constant headache, occasional vertigo, tinnitus aurium, failing appetite and chronic diarrhœa. There has been at times some œdema of the ankles and face, but not constant. During the past two months there has been a marked febrile attack almost every afternoon, lasting several hours. The amount of urine passed has been very large, especially during the night. There has been no vomiting, no shortness of breath, though there has been slight dyspnœa, and no pain anywhere, except in the head, at any time. During the past four months the vision in both eyes has steadily and somewhat rapidly grown worse, the impairment being most marked in the left eye. For the past year, there has been no treatment of any kind.

When first seen the most marked symptom was the complexion, which was startling in its blanched appearance. The skin of the face and neck was dead white and apparently completely bloodless. The lips and conjunctivæ were almost colourless. The pupils were widely dilated and very sluggish. Radial pulse thready and 90 in the minute. Respirations 20 in the minute, slight but regular. Heart's action feeble but regular. Respiratory murmur heard feebly all over the chest, front and rear. Tinnitus aurium very annoying and constant. Hearing power apparently undisturbed. Drum heads about normal in appearance, and Eustachian tubes freely open.

No central vision with either eye. Eccentrically with nasal side of the retina, right eye $V=\frac{6}{100}$; left eye $V=\frac{3}{100}$; no improvement by any glass. The ophthalmoscopic examination showed a rather uncommon picture. The whole fundus as far forward as the ora serrata presented a brilliant dead white colour, strewn with red spots and lines which proved to be hemorrhages. The optic disk was invisible, but the vessels could be seen converging, though they disappeared at times from view in the infiltration. The infiltration was most dense at the macula and optic disk, and gradually thinned out towards the periphery, there being a difference in elevation of nearly $\frac{1}{24}$. The hemorrhages were most numerous on and near the disk, and were much larger here, some of them being great blotches, though they existed all over the fundus in the course of the venous branches. The symptoms were all most marked in the left eye, but there was no red reflex at any point in either eye. The retinal veins were enormously distended and tortuous, and the arteries in places very much diminished in calibre.

The urine was very light coloured, acid, sp. gr. 1010, contained a large amount of albumen, deposited only a slight precipitate on standing, and contained numerous hyaline and fatty casts. About 11 grains of urea to the fluidounce. No pus nor blood-corpuscles. The quantity passed in the twenty-four hours was very nearly two gallons.

An examination of the abdomen showed that both liver and spleen were enlarged, especially the former. There was no tenderness over any portion of the abdomen, but there was in the lumbar region on pressure. An examination of the blood showed a perceptible though not marked increase in the number of the white corpuscles.

The patient had no appetite, the diarrhœa was quite profuse, and a very unfavourable prognosis was therefore made. She remained, however, under observation from early in January till March 3d, when she died. During this interval she was seen every second or third day, but there were few changes to note. The retinal hemorrhages recurred again and again, and no treatment seemed to avail to stop them. The infiltration remained unchanged till the last, and vision very slowly grew worse. During the first part of February the diarrhœa was somewhat checked, and the amount of urine voided was reduced almost to the normal standard. The albumen also diminished very much in amount, and the casts became fewer. But in the last week in February the amount of urine was largely increased and it became loaded with albumen, though the casts were not materially increased in number.

The patient became suddenly comatose on March 2d, and died on the morning of the 3d. No autopsy was permitted.

In this case the infiltration of the retina was entirely different from that which is met with in the so-called retinitis albuminurica, which occurs in detached masses usually in the vicinity of the disk and macula. This was a continuous dense infiltration reaching from macula to ora serrata without a break, and resembled the exudation met with in cases of suppurative choroiditis occurring in cerebro-spinal meningitis or in general pyæmia, except that the infiltration was in the retina. The numerous and extensive hemorrhages also distinguished it from the latter, and certainly pointed to degeneration of the coats of the vessels. In view of the history of the case, the long-continued necrotic process in the bone, the later renal disease, probably at first lardaceous and subsequently becoming fibrous, producing the contracted kidney, is it not possible that the coats of the retinal bloodvessels, and subsequently the retina itself became infiltrated with this same lardaceous material? The appearances shown by the ophthalmoscope were more pronounced and extensive than the writer had ever seen before in the retina, but early in the same month in which the death of the first patient occurred, a second patient presented himself with almost the same condition of the retina, as follows:—

Case II.—James F., æt. 26, single, sailor, first seen early in March, 1879. The patient is tall, fairly nourished, but of marked strumous diathesis. Has never had syphilis, rheumatism, or malaria. Eight years ago received a severe blow on the left shin from a chain, which bruised the skin extensively and injured the bone to such a degree that necrosis set in and the wound has been open and discharging ever since. He has never had any continuous systematic treatment, and no operative interference has ever been attempted. Small pieces of bone have come away in the purulent discharge at different times. About four years ago he began to be troubled with nausea and headache, with occasional attacks of vertigo.

He also complained of blurring of his sight and of some dyspeptic symptoms in addition to the nausea. For several years, he does not know how long, the flow of urine has been markedly increased, so that he was obliged to rise several times at night. About six months ago the blurring of his vision, which had been transient, became permanent and his sight has steadily grown worse, until for the past month he has moved about only with great difficulty and danger. When he presented himself, the most marked feature was here, as in the first case, the complexion. The colour was a dead, pasty-white, of the same tint throughout, and this extended down upon the trunk and limbs. The conjunctiva, lips, and buccal mucous membrane were almost bloodless. The heart's action was feeble and irregular, and there was a well-marked murmur at the base with the first sound. Pulse 96 and feeble. Respiration 30 in the minute, labored, and each inspiration hurried. Auscultation and percussion showed a small amount of fluid in the left pleural cavity. The patient's liver was enlarged to a marked degree and was sensitive to pressure, and he said he had had an obstinate diarrhœa for several months, but that just at this time it was better. He still passed about six quarts of urine daily, which was very pale in colour, had a slight deposit on standing, was acid, sp. gr. 1012. It was loaded with albumen, and contained large numbers of hyaline and fatty casts.

Right eye V = $\frac{4}{200}$ eccentrically.

Left eye V = movements of the hand eccentrically.

Vision in this case was not limited to the nasal halves of the retina, but extended irregularly in all directions towards the temporal side. An ophthalmoscopic examination revealed almost the counterpart of the eyes of the first patient, but with a difference. In the *left* eye the infiltration was continuous and solid from macula to extreme periphery, of a dead white colour, interspersed with numerous red blotches, some old, others recent, which were hemorrhages from the retinal vessels. In the *right* eye the infiltration was not continuous from macula to periphery, but there were patches of red choroid visible. Wherever the infiltration existed, however, it was of the same dense white colour, and in this eye also were numerous hemorrhages, some of them quite large. In both eyes the optic disks were not distinguishable, and their situation could only be told by the convergence of the vessels. In places the vessels would disappear, being covered by the infiltration.

Judging from this second case the infiltration first occurs near the nerve and macula, and subsequently invades the whole of the retina.

In the lower third of the left tibia, near its junction with the middle third, was a ragged, unhealthy ulcer leading down to the bone, its edges elevated, uneven, and purple, and all the tissues in the vicinity were swollen and infiltrated. A probe passed into the tibia upward nearly two inches through a large cavity, and about an inch in all other directions. Dead bone could be felt everywhere, and the end of the little finger introduced into the opening, discovered a loose piece of bone, evidently a sequestrum of some size. The discharge from this hole had been profuse, though thin, and still continued.

The patient's condition was precarious, and his friends were told that he might die at any moment. He lived, however, for nearly two months in about the same condition, though his strength steadily failed. The eyes remained unchanged, except that fresh hemorrhages recurred repeatedly. The nausea towards the end was brought on by every attempt to introduce

food into the stomach, though brandy was not rejected. The flow of urine diminished somewhat, but the amount of albumen and the casts remained about the same. He grew comatose two days before death and remained so till the end. In this case also it was impossible to obtain an autopsy. The amount of urea was not determined in this case. The blood was examined, and an increase in the number of the white corpuscles was noted.

A study of these two cases seems to furnish strong evidence of the production of lardaceous disease of the liver and kidney by chronic suppuration in bone tissue with extensive necrosis. It is highly probable that in both cases the primary lardaceous change in the kidney subsequently gave place to a fibrous degeneration with contracted kidney and possibly contracted liver. The retinal disease was in both cases a late complication, and the infiltration was very different from that ordinarily met with in the retina in chronic interstitial nephritis. Albuminuria occurring in cases of long-continued suppuration, or in tuberculous, strumous, syphilitic, or malarial cachexiæ, and accompanied by hypertrophy of the liver and spleen, causes a strong suspicion of lardaceous disease. If with *Cohnheim* and some later authors we regard this change as a degeneration, we must recognize it as directly taking the place of the normal protoplasm of the cells, muscular fibres, capillary walls, etc. The process, be it infiltration or degeneration, appears almost always in the course of a general disease of pronounced progressive character, which is not limited to a single organ. Whether *Cohnheim* is correct in regarding it as a local degeneration produced by general causes, in which the amyloid substance arises directly from the pre-existing albumen of the tissue, remains still a moot point. *Wagner* regards the lardaceous disease as in all probability a link between albuminates and the fats and cholesterine. As regards the suggestion of lardaceous infiltration of the retina made in the two cases reported, we must recollect that the retina is largely made up of connective tissue, and that lardaceous infiltration of this tissue is a point in pathology still unsettled. At the same time the retina is a highly-developed nervous tissue, and lardaceous disease of nerves has been reported in a number of instances as actually found, so that its occurrence in the retina is certainly possible.

Dr. Dickinson holds the view that the special change is an infiltration of the tissues by a material foreign to their healthy nature, which in all probability is brought to them by the bloodvessels, but in this view he stands almost alone among English pathologists. As regards the causation, most writers attribute the change to but two causes, viz.: chronic suppuration and syphilis. Of 83 cases of lardaceous disease collected from the post-mortem records of St. George's Hospital, 73 were in connection either with protracted suppuration or syphilis; of these, suppuration occurred in 62 and syphilis in 18.

Dr. C. Turner found a total of 58 cases of lardaceous disease in about 2200 autopsies, and of these there were only 10 in which the disease was not clearly associated with suppuration or syphilis.

According to *Dr. Hilton Fagge*, there occurred in Guy's Hospital 244 cases of lardaceous disease in 20 years, and of these 154 were due to suppuration without syphilis, and 76 were due to syphilis. Of the latter 34 had bone-disease, leaving 42 cases presumably due to syphilis alone.

As to the way in which suppuration produces the disease, there is an enormous loss of certain constituents of the blood, notably of the white corpuscles, carrying away the potash, and the lardaceous material may be regarded, according to *Dickinson*, as a deposit from the residuum. But in the two cases reported by the writer, there was a slight increase in the number of the white corpuscles instead of a loss.

When we come to consider syphilis as the cause, we are still unsettled as to its mode of action. Of course syphilis involves injury to nutrition in a variety of ways. *Dr. Greenfield* has seen lardaceous disease well-marked in both congenital and acquired syphilis, without any antecedent suppuration. On the other hand *Mr. Hutchinson* deems it improbable that the mere existence of a syphilitic taint could produce the disease without the intervention of a suppurative process. He is inclined to accept one of two explanations of the process; either that the protracted suppuration attendant on certain severe forms of syphilitic ulceration of skin and bone produces general lardaceous tendencies, just as other prolonged forms of suppuration would, or else that syphilitic gummatous formations are themselves locally liable to lardaceous changes. He recognizes the fact that syphilitic patients occasionally fall into a hopeless cachexia, and that here extensive lardaceous changes are believed to have taken place, but he believes that severe suppuration always precedes the cachexia.

In an interesting paper by E. Bull in the *Nordiskt Medecinskt Arkiv*, Bd. X., 4de Häftet (Nogle Kritiske Betragtninger over den amyloide Degeneration, særlig med Hensyn på dens Varighed og dens Forhold til den Bright'ske Retinit), the author holds that the kidneys are the earliest and most severely affected by amyloid disease of all the organs in the body, and that the disease is immediately marked by albuminuria. In the greater number of cases its duration is as a rule less than a year, and sometimes only a few months. Exudative retinitis he believes does not occur in uncomplicated amyloid degeneration. He also thinks that the cases of long duration of amyloid disease, which have been reported, are due to a faulty conception of the pathological process. They should be regarded as cases of primary renal cirrhosis with subsequent amyloid degeneration occurring towards the end of life. These views are not new, and are the ones generally held now by the profession. They point strongly towards the improbability of retinal complications in pure amyloid disease of the kidneys, and indirectly against any such degeneration of the retina as has been suggested in the two cases reported in this paper. These cases were, however, ophthalmoscopically unique of their kind, at least in the experience of the writer, nor has he seen a report of any similar case. It is not known

in what condition the retina was at the beginning of the infiltration, and it is possible that the exudation began as in ordinary Bright's retinitis; but its course and termination were totally different, and the supposition advanced seems not unreasonable, though it is novel. Of course the crucial test, microscopic examination of the infiltrated membrane, is wanting, and hence the histories are defective.

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